

Amendment and Response

Serial No.: 09/600,392

Confirmation No.: 4850

Filed: September 8, 2000

*For: AN AUTOREGULATORY SYSTEM FOR VALIDATING MICROBIAL GENES AS POSSIBLE
ANTIMICROBIAL TARGETS USING A TETRACYCLINE-CONTROLLABLE ELEMENT*

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infecting a plurality of mammals with a microbe that has been genetically altered such that the amount of said gene product produced by said genetically altered microbe is regulated by a Tetracycline-Controllable Element (TCE);

where said TCE is a gene regulatory system that controls the expression of the target gene product through its ability to modulate the function of said gene in response to said microbe's exposure to tetracycline, and where said TCE is comprised of a tetracycline-controllable transcription promoter polynucleotide sequence;

where said genetically altered microbe also comprises a polynucleotide sequence encoding a tetracycline resistance protein;

exposing the plurality of mammals to tetracycline;

once an infection with the genetically altered microbe is established, removing the tetracycline exposure of a portion of the plurality of mammals, such that a first group of the plurality of mammals is exposed to tetracycline and a second group of the plurality of mammals is not exposed to tetracycline; and

comparing the degree of infection, microbe levels, or survival rates of the mammals in the first group and the second group wherein a mathematically significant difference between the two groups of animals in the survival rates, levels of microbes, or levels of infection present identifies the gene product as important to a microbe's ability to infect or sustain an infection in a mammal.

9. [AMENDED] The process of claim 1, where said mathematically significant difference between the two groups of animals is a mathematically significant difference in the levels of microbes or levels of infection present in the mammals.

10. [AMENDED] The process of claim 1, where said mathematically significant difference between the two groups of animals is a mathematically significant difference in the survival rates of the groups of animals.

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11. [AMENDED] The process of claim 1, where said mathematically significant difference between the two groups of animals shows that animals exposed to tetracycline have poorer health, higher rates of infection, lower survival or higher levels of microbes than animals not exposed to tetracycline.

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